FÜTTERER (G.)

Primary Carcinoma of the Gall-Bladder.

BY

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PRIMARY CARCINOMA OF THE GALL-BLADDER.

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Although quite a number of cases of primary carcinoma of the gall-bladder have been published, yet the writer thinks that more publications of such cases are necessary in order to bring out points not yet clear to us.

The case here described has several interesting features, not only in reference to the findings in the gall-bladder but also to the surrounding and more distant portions of the liver.

History.—A female, married, 47 years of age, was admitted to the German Hospital, where she came under my care December 3, 1896. The patient's father died at the age of 70 years; her mother died of typhoid fever in younger years, the exact age being unknown. Four brothers and a sister are living and well. One brother died during childhood, and another in later life after a period of insanity lasting two years.

The patient was the mother of one child, which died in infancy. She had been very healthy excepting measles at the age of eight years and malaria at the age of eleven. She reached her menopause two years ago. Her bowels were always regular and her appetite good, but three months ago she had a short attack of jaundice.

Her present illness commenced three weeks before she was admitted to the hospital, with intermittent attacks of pain in the region of the liver. She became icteric, the stools being discolored, and she remained in this condition until I saw her, at which time she was deeply jaundiced. As the patient had a well developed panniculus adiposus, the lower border of the liver could not be easily determined, but on deep percussion over the umbilicus, and reaching several inches to the left of it, there was a marked flatness of sound which I thought was due to an enlargement of the liver. Over the heart, the left part of which was somewhat enlarged, a murmur—mainly systolic, but also diastolic—was to be heard. The pulse was rather small, 82 per minute, while the temperature was 100° and ranged between 100° and 99 1-5° for the next five days.

The diagnosis was chronic endocarditis with valvular lesion of the aorta and probably gall-stones and cholecystitis.

As the pains were very severe, hypodermic injections of morphine had to be given daily. With a view of disinfecting the gall-ducts and bladder, oil of wintergreen was ordered to be given every

two hours. The use of oil of wintergreen for this purpose is rational, as it contains methylsalicylic acid ($C_7H_5(CH_3)O_3$), and it has been shown by Stadelmann that salicylic acid is discharged by way of the gall-ducts. I gave the oil until dizziness appeared, and would then wait a day or two and repeat it.

On December 8 the patient was transferred to the surgical ward, and on the 9th of December she was at my request operated upon by Dr. Weller Van Hook and three faceted gall-stones removed from the gall-bladder. Fig. 1 shows a picture of the gall-stones, giving

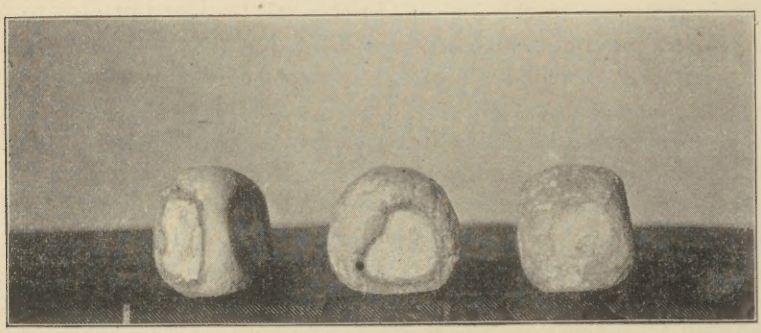

FIG. 1.—Gall-stones removed from gall-bladder. Natural size.

their exact size. The stones had so many facets that it was suspected that some were missing, but none could be found. The gall-bladder was about two-thirds normal size; it had a slightly milky appearance and was overlapped by a nodule of about four centimeters diameter, which was located in the lower margin of the liver and which—as was later proved by microscopical examination—was of carcinomatous character. The liver itself was of a deep purple color, with an uneven surface and small nodular elevations, caused by dilated gall-ducts as has been observed by Fenger.

Above the umbilicus, and to the left of it, quite a number of enlarged glands could be felt and also an enlarged pancreas, the presence of the former explaining the area of dulness which had been erroneously believed to indicate an enlargement of the liver.

The patient died December 12, and the post-mortem examination revealed the following: A hemorrhage from the wound had filled the gall-bladder, had forced its way downward under the parietal peritoneum, and had entered the abdominal cavity and almost filled the pelvis. The liver was a pale yellow, of about normal size, and did not show the small nodules which had been seen on its surface during the operation. As already mentioned there was a

small, hard nodule of grayish color in that part of the lower margin of the liver which overlapped the somewhat contracted gall-bladder. The gall-bladder itself showed a milky thickening of uniform character due to a chronic fibrous cholecystitis. There was a small tumor, partly filiform and partly nodular, at the neck of the bladder near its attachment to the liver. The mucous membrane proper had here been forced upward by a hemorrhage, the extent of which can be seen in Fig. 2. From here the cancerous growth had passed over to

FIG. 2.—The nodule in the uppermost part of the picture shows carcinoma growing in the direction of the hepatic duct. Below and to the right of this is a shaded portion showing hemorrhage. Further along this border are seen the corrugations of mucous membrane of the gall-bladder. The extreme right of the figure shows metastatic carcinoma.

the hepatic duct, filling out the space between it, the gall-bladder and the cystic duct. It had reached the upper end of the hepatic duct, causing a thickening of its walls, thus bringing about stagnation of the contents of the bile-ducts inside of the liver, and causing a considerable dilatation of the larger ramifications of the hepatic duct inside of the liver; they were filled with an almost clear mucus in which no bile was visible, while the liver substance presented an extremely icteric condition. The walls of the ducts were visibly thickened and of a milky appearance. No carcinomatous masses were to be found in any portion of the liver except those surrounding the gall-bladder and the hepatic duct. The cystic duct was practically closed, and the common duct showed a normal appearance.

The carcinoma had not only grown upward but also downward

to the margin of the liver, there forming the nodule which has already been mentioned. The glands around the porta hepatis were swollen, and this was also the case with the retroperitoneal glands. The left ventricle of the heart was enlarged; the aorta and its valves were calcified, and several fibromata were found in the uterus. No carcinomatous growth was found elsewhere in the body.

Microscopical Examination.—During the microscopical examination of the walls of the gall-bladder somewhat distant from the carcinoma I found mucous glands, a fact which is worth mentioning for several reasons. Henle (*Handbuch der Systematischen Anatomie des Menschen*, vol. ii, 1873, page 225) mentions that mucous glands in the walls of the gall-bladder are rarely found. Theile, Wedle

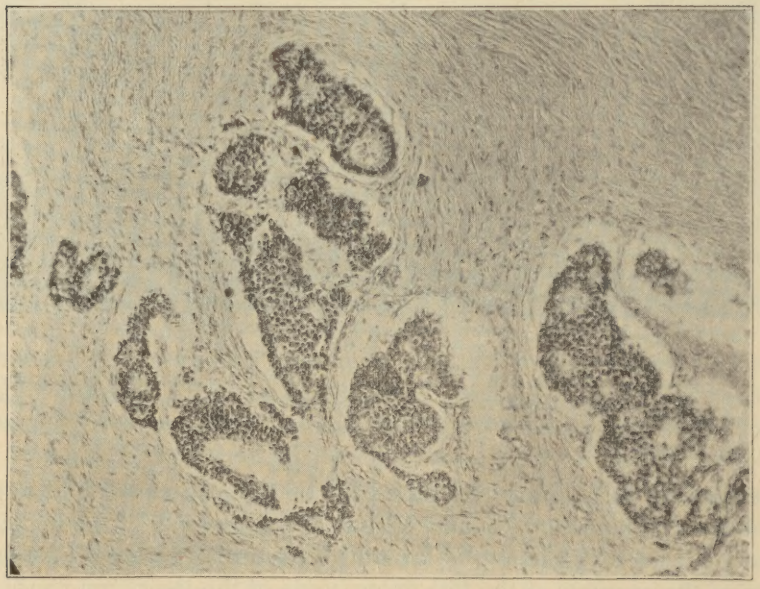

FIG. 3.—Glandular carcinoma in the second layer of the gall-bladder.

and Kölliker did not find them. As the examination progressed it could at last be seen that the carcinoma had originated from glands in the mucous membrane of the gall-bladder at its neck. The structure of the growth was, as Fig. 3 shows, of an extremely glandular character. Fig. 4 demonstrates the growth of the carcinoma from the wall of the gall-bladder, against the liver substance, forcing the latter back; but in other portions it was found that the carcinoma had also entered the blood-vessels and caused adjacent metastases. Although the carcinoma was of recent date, yet metastases were

already present in the portal glands as shown by Fig. 5. Other glands were not subjected to microscopical examination. The writer thinks it unnecessary to go into further detail in the description of

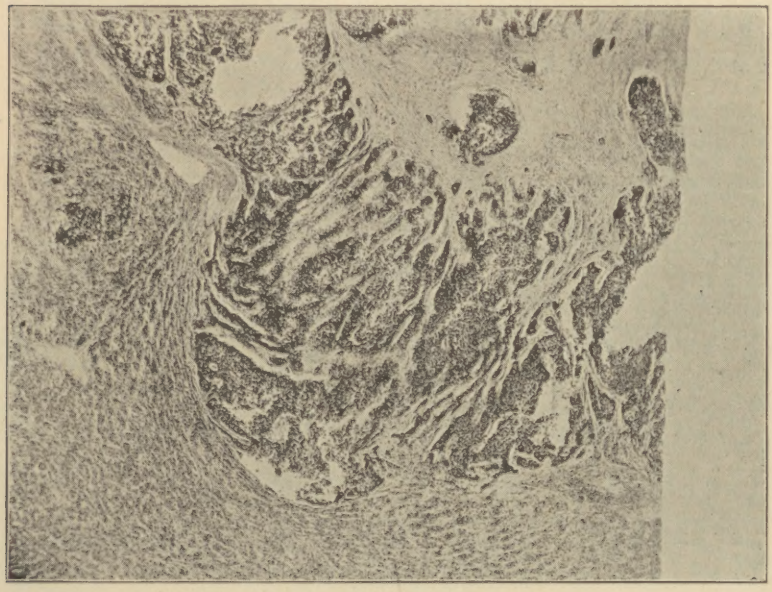

FIG. 4.—The upper right-hand portion of the figure shows the second layer of the gall-bladder, from which springs a glandular carcinoma, compressing the liver substance.

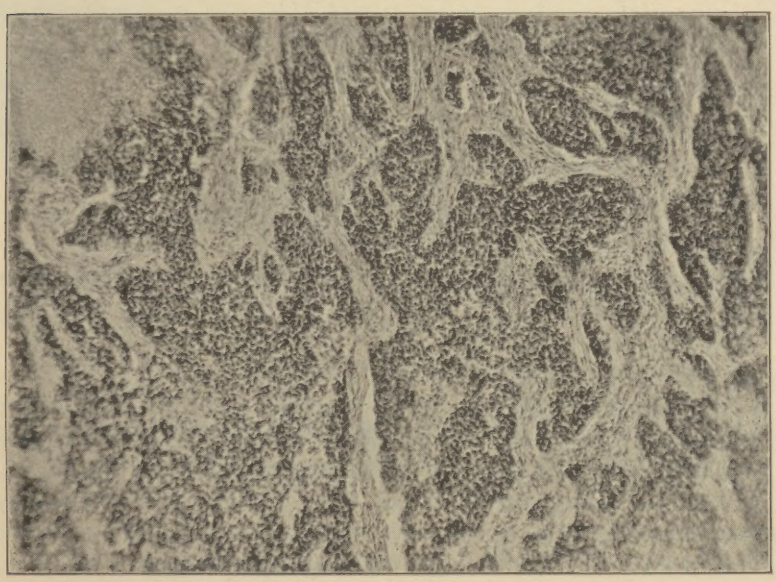

FIG. 5.—Metastasis of the carcinoma in a portal gland.

the microscopic appearances, as the cuts illustrate those so well. The microscopical examination of the dilated gall-ducts (Fig. 6) and their relationship to the liver substance showed the following: The bile-ducts which are found in Glisson's capsule show fibrous thickenings of their walls, the surroundings of the latter also showing an increase of connective tissue and some cellular infiltration.

FIG. 6.—Dilated gall-ducts inside of liver laid open. To the right is seen the duodenum and papilla; leading from this is the common duct. The cord-like structure in lower portion of figure is the contracted cystic duct. The greater portion of gall-bladder has been removed for microscopic examination.

Occasionally small portions of necrotic liver substance were found, as seen in Fig. 7. The necrotic areas were, I believe, caused by pressure of the dilated gall-ducts against the liver substance. These not only show necrosis, but also beginning regeneration, represented by bunches of newly formed gall-ducts growing through the necrotic areas into the surrounding normal liver substance.

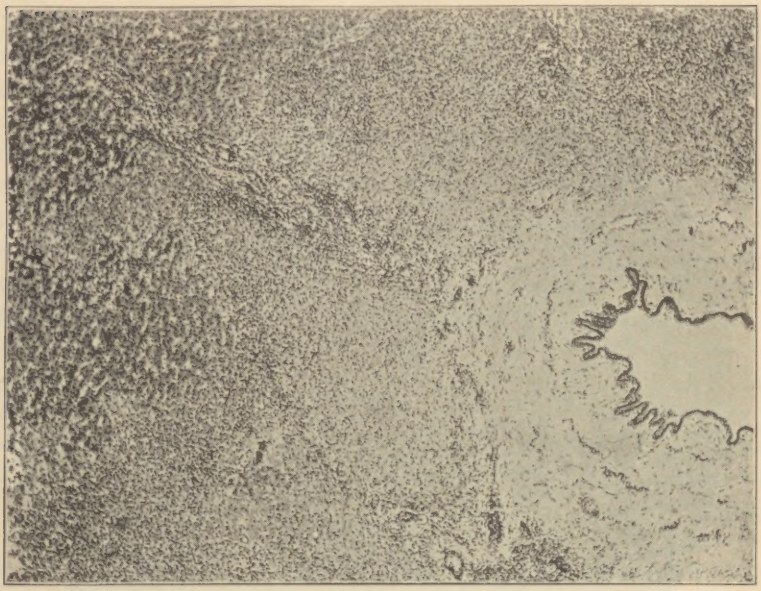

FIG. 7.—To the right is shown a dilated gall-duct surrounded by areas of necrosis due to pressure. To the left is normal liver tissue, and extending across the figure a newly formed (regeneration) bile-duct can be seen growing into the healthy liver substance.

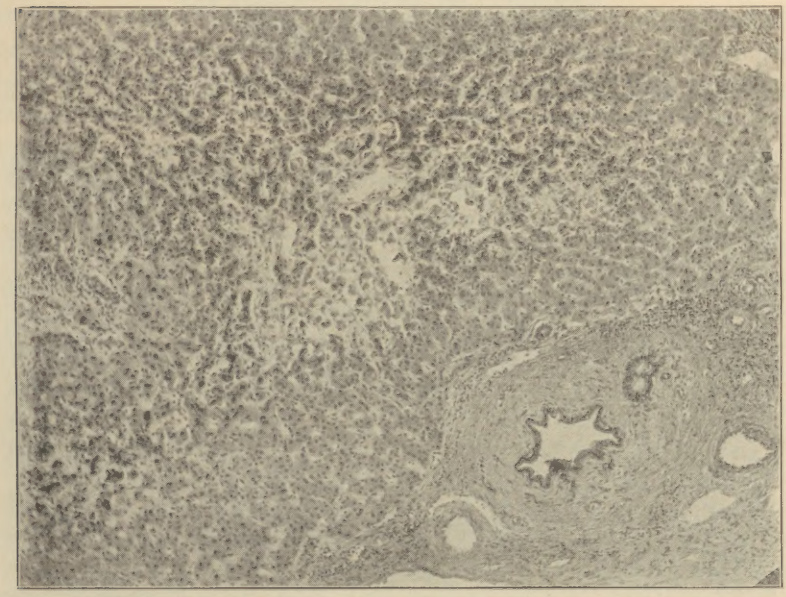

FIG. 8.—Liver cells in various stages of degeneration. The darker portions represent nearly normal tissue, while the lighter shading shows the degree to which degeneration has advanced. In the microscopic specimens these areas were stained an intense yellow.

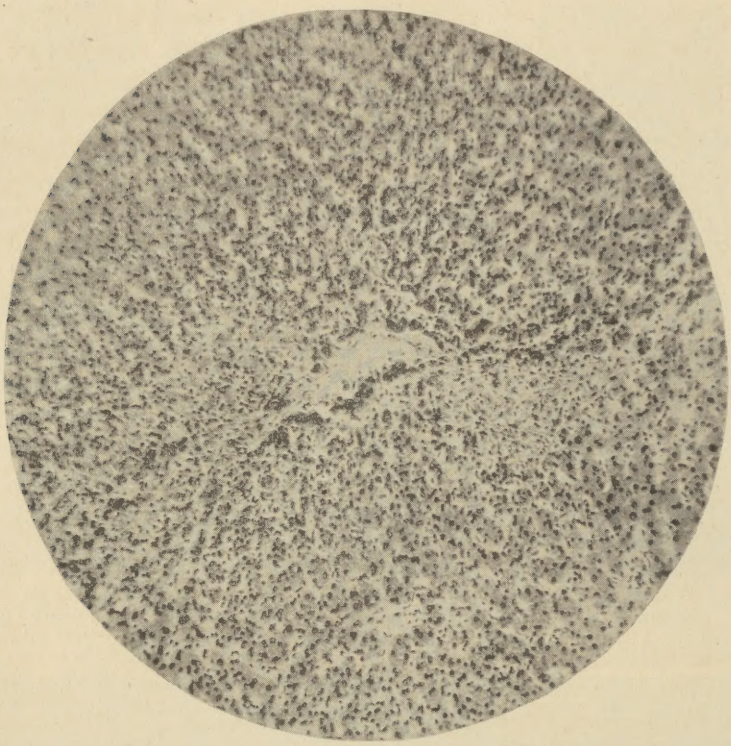

FIG. 9.—The centre shows a cross-section of a central vein surrounded by a layer of well preserved liver cells. Outside of these well marked areas of necrosis can be seen.

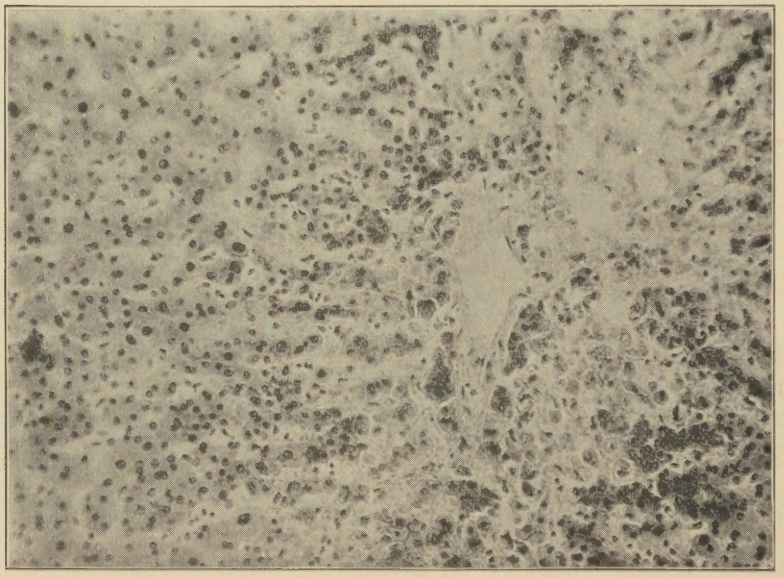

FIG. 10.—Transverse section of central vein, with areas of complete dissolution of liver cells (icteric necrosis).

Again, as Fig. 8 demonstrates, there were places where the dilated and thickened gall-duct had not caused pressure necrosis, so that the necrosis has occurred irregularly, in spots. Fig. 9 shows a second kind of necrosis which was found rather uniform through the whole liver, surrounding almost every branch of the central veins—an icteric necrosis which had caused almost entire dissolution and an almost total degeneration of the liver substance, especially that surrounding the central veins. Fig. 10 demonstrates this condition well. These parts in our microscopic specimen appear extremely yellow, while the intermediate and peripheral zones of the ascini show, in general, a perfectly normal appearance.

Epicrisis.—As Fig. 1 shows, the three gall-stones found in this case must have been of long standing, while the carcinoma was of recent date. It will be remembered that the patient had an attack of icterus three months before she was admitted to the hospital and that this disappeared, returning again three weeks before her admission. As carcinoma of the gall-bladder grows rather rapidly, it is not to be supposed that at that time there could already have been a narrowing of the hepatic duct caused by cancer; it must be believed that a stone or two left the gall-bladder and passed through the common duct, thus causing a temporary obstruction and icterus, and that the carcinoma is of more recent date. As carcinoma of the gall-bladder generally originates from the epithelium of the mucous membrane, it is very interesting to note that this one originated from the mucous glands. Dilatations such as we have found here, involving the gall-duct system in the liver, have been observed in a number of cases, and it has also been stated that they were filled with mucus instead of bile.

The opinion has been advanced by Courvosier, that atrophy of the liver causes a non-production of bile, and that therefore no bile can be excreted. In this case, however, there are only small atrophies of liver substance caused by pressure of the gall-ducts and the icteric atrophies of the central portions of the ascini. That the liver produced bile in large quantities was demonstrated by the icteric coloring of the liver and the dark icteric coloring of the whole body. The latter received the surplus of bile produced by the liver. It seems to me that the course of the bile has been reversed for some reason, so that instead of running into the gall-ducts to the peripheral portions of the ascini, it was forced towards the lymphatics which surround the central veins. In this way the intermediate and peripheral portions of the ascini got rid of the bile almost as fast as it was produced, while the central portions were

continually overloaded with it; and so caused a dissolution of the cells. If this condition had existed for a longer time the icteric mucoses would gradually have crept towards the peripheral portions of the ascini, and it may be that Courvosier's specimen, from which he drew his conclusions, represented such a condition. As Courvosier's book is not at my command, I am unable to form a correct opinion as to his findings.

The causes which prevented the bile from entering the gall-ducts have been two: first, the counter-pressure by the stagnating mucus inside of the gall-ducts; and second, an obstructed communication between the gall-capillaries in the ascini and the gall-vessels in Glisson's capsule. I rather believe that the latter was the main cause, but this is not susceptible of proof. It would be of positive value if we knew that the removal of an obstacle would be followed by a prompt discharge of bile; while in the second case there would have been an apparently irreparable condition.

Literature.—In order to give the reader a general idea of this condition, I append short histories of a number of cases, but for a more intimate study I should recommend the writings of Musser, Courvosier and others.

Auetsch: Woman of 49 years had a gall-bladder fistula through which a great number of gall-stones were discharged. Three years later the patient died, and the post-mortem revealed a primary carcinoma of the gall-bladder with compression of the common duct and dilatation of the gall-ducts, which were filled with a milky fluid. The central portions of the ascini appeared dark green, the peripheral areas being lighter.

Durand: Fardel, between 1838 and 1840, saw six cases of primary carcinoma of the gall-bladder, all in women over 60 years, and one over 80 years of age. In three cases there were no changes in the neighboring organs, while in the other three the carcinoma had involved the parts surrounding the gall-bladder and had caused metastasis. In all cases the gall-bladder contained gall-stones. The disease lasted from four to five months in five cases and almost two years in the sixth. Jaundice well marked in four cases, not well marked in one, and none in one.

W. Pepper saw a case of scirrhus of the gall-bladder and of the pancreas, lasting for nine months.

Paulicki observed a primary carcinoma of the gall-bladder in a 30-year-old servant girl. Icterus came rather late, and post-mortem revealed a primary carcinoma of the gall-bladder, secondary carcinoma of the liver, and a very much distended gall-bladder with

large stones. The cystic and common ducts were infiltrated by carcinomata, their walls being thickened and their lumen narrowed.

Coraza: Carcinoma size of a fist, adherent to the transverse colon; carcinomatous degeneration of liver; gall-bladder contained twenty gall-stones.

Carpentier: Tumor of the gall-bladder with gall-stones and icterus. Woman died, after the disease had lasted fifty days, with coma cholæmicum. Carcinoma of gall-bladder, secondary carcinoma in the liver, and gall-bladder filled with large stones.

Haas: Two cases of primary carcinoma of the gall-bladder; gall-stones in one case, perforation of gall-bladder, peritonitis, death.

Heurot: Primary carcinoma of gall-bladder; woman, 49 years; icterus. Disease lasted eight months. The lower surface of the liver, the gall-bladder and the gall-duct were imbedded in carcinomatous masses which were adherent to the small curvature of the stomach and the duodenum. Gall-bladder contained about fifty gall-stones.

Planteau: Primary carcinoma of gall-bladder with compression of the cystic and hepatic ducts, chronic icterus and ascites, in a woman of 39 years. Liver evenly green, large, adherent to the diaphragm, strongly cirrhotic; liver parenchyma soft and fragile. At the fundus of the gall-bladder, carcinomatous degenerations; a carcinomatous nodule at the junction of the cystic and hepatic ducts; the latter two ducts and the bile-ducts in the liver were dilated. Choledochus normal; arteria hepatica and vena portæ imbedded in carcinoma; lymphatic gland at the porta hepatis infiltrated.

Remy: Woman, aged 38. Death at about eight months. Liver of normal size, about ten white nodules in anterior margin the size of cherries. A lobulated, hard white mass extended from the gall-bladder and porta hepatica to duodenum and pancreas. Ductus choledochus could not be found; vena portæ was pushed aside. The shrunken gall-bladder contained a small gall-stone; its fundus showed carcinomatous degeneration, and the diameter of its wall was four centimeters.

Cohn: Five cases in women between 40 and 60 years; one case, a woman of 77 years. Disease lasted from five to twelve months. In five cases sooner or later icterus; in one none. In five cases ascites. In five cases primary carcinoma of gall-bladder and secondary carcinoma of liver, while in one case the liver was unchanged. In four cases stones in the gall-bladder; in one, a large number of stones in the gall-ducts. In the oldest patient there were no stones.

Krauss: *Case 1.*—Woman, 48 years. Duration five months. General anemia and cachexia, edema of the lower and upper extremities, primary carcinoma of the gall-bladder, which had grown over the pylorus and duodenum. Large carcinomatous cavity between stomach, duodenum and gall-bladder, the right lobe of the liver, which was adherent to the front wall of the chest, and the omentum majus, which was turned upward and adherent; liver full of carcinomatous nodules of the size of apples, one of which had grown into the diaphragm; nodules in ascending colon, which was adherent to the liver; considerable dilatation of the stomach; encapsulated peritonitis exudate (gas) between the transverse colon, which sunk down, stomach and side wall of the abdomen connecting with the carcinomatous cavity.

Case 2.—Woman, aged 43; slight icterus; carcinoma of gall-bladder which was filled with stones, adherent to colon; gall-ducts free; liver full of carcinomatous nodules; carcinomatous degeneration of lymphatic glands at the porta hepatis.

Case 3.—Man, aged 45. Primary carcinoma of gall-bladder with extensive metastasis in the abdomen and pelvis, the right inguinal gland, liver, stomach, and right lung; biliary cirrhosis, dilatation of the gall-ducts, and retention of bile; cholelithiasis. Diphtheritic inflammation of the mucous membrane of the whole large intestines and the lower part of the ileum; edema of the lungs and very marked general jaundice.

Case 4.—Woman, 42 years. Primary carcinoma of the gall-bladder extending into the liver; compression of the hepatic duct by a portal carcinomatous degenerated lymphatic gland; marked icterus; lobular pneumonia; cicatrix in spleen with calcareous deposits, nephritis, fresh pericarditis; hemorrhages on inner surface of dura mater. Gall-bladder dilated, filled with slimy green bile and a number of stones; gall-ducts of the liver filled with a whitish, opalescent slimy liquid. This case lasted about three months.

Case 5.—Woman, 47 years. Primary carcinoma of the gall-bladder extending into the liver and the porta hepatis; thrombosis of some of the veins of the liver with compression of the common duct; biliary cirrhosis; embolism of the pulmonary artery in the right lower lobe with hemorrhagic infarction; icterus.

Delano Ames: *Case 1.*—Woman, aged 47 years. Primary carcinoma of gall-bladder; pains and tumor in right hypochondrium. Absence of jaundice; profound anemia. Obstinate constipation for four weeks before death. Death from exhaustion six days after exploratory incision. Gall-stones.

Case 2.—This was a woman 54 years of age, upon whom no post-mortem examination was made.

Case 3.—Woman, 52 years of age. Primary carcinoma of gall-bladder, which gave a nodular mass, definitely felt on palpation. The gall-bladder was thickened and contained about 100 small stones. There was great induration about the common duct, at the head of the pancreas and in the gastro-hepatic omentum. The common duct passed through the mass and was almost occluded. The liver weighed only 1500 grammes and presented numerous medium-sized cancerous nodules throughout its substance.

Siegert (Zur Aetiologie des Primären Gallenblasen Carcinoms. *Virchow's Archiv.*, bd. 132, 1893): Seven cases of primary carcinoma of the gall-bladder; among them a very small one showed cholelithiasis with chronic cholecystitis. From 99 cases gathered from literature, and his own 7 cases, 14 were in men and 83 in women, with gall-stones in 94 cases; three times they were missing and twice their presence was not ascertained with certainty, owing to a fistula between gall-bladder and colon. Of fourteen cases of secondary carcinoma of the gall-bladder observed by Siegert, ten were found in men, and gall-stones were only found twice. Siegert agrees with Klebs and Zenker, who believe that the gall-stones are primary, and that carcinoma follows the chronic changes of the wall of the bladder, caused by the stones.

T. N. Kellynack (*The Practitioner*, London, 1896) reports Brockbank's proportion of gall-stones as 22 per cent. in females and 12.5 per cent. in males.

C. F. Martin: A case of primary cancer of the gall-bladder. The gall-bladder was much diminished in size; the wall of grayish-white color, and very much thickened, especially near the attached margin. Toward the lower and outer portion was a perforation one centimeter in diameter with round smooth edges, and through this the gall-stones evidently had escaped. Where the gall-bladder was thickest there was much new tissue formed, connecting the gall-bladder and the liver substance; it extended irregularly into the adjacent liver substance, being apparently continuous with and arising from similar conditions of the gall-bladder itself. The average diameter of this irregular area was about four centimeters. The liver tissue in the immediate vicinity presented a few smaller nodules of the same character. Elsewhere the liver contained about nine or ten grayish-white rounded nodules of comparatively small size, all firm on section and not penetrating deeply into the tissues of the organ. Many of the bile-ducts were distended.

On microscopic examination the walls of the gall-bladder showed chronic fibroid thickening, the mucosa in some parts necrosed, and in others deep irregular proliferation of epithelial cells of a distinctly glandular type; the nodules in the liver showed the ordinary condition of metastatic glandular carcinoma. The periportal glands were distinctly cancerous.

Graham (*Canadian Practitioner*, 1895): A male. Primary carcinoma had destroyed the gall-bladder and caused metastasis all through the liver. Gall-stones in the gall-bladder. No evidence of carcinoma in any other part of the body.

Geo. Dork (*University Med. Mag.*, Philadelphia, 1895, 90–95): Woman, aged 47. Carcinoma of the gall-bladder with gall-stones. No jaundice.

Riedel reports three cases of carcinoma of the gall-bladder with stones. All three patients were females, 56, 58, and 56 years of age respectively. The third patient experienced a pressure in the region of the stomach lasting for years. Six weeks before operation she fell, striking the right costal arch, and since then had pains in that region.

Historical.—Delano Ames, who has gathered a great deal of literature on the subject of primary carcinoma of the gall-bladder, may be cited in reference to the historical development of our knowledge on the subject. He says: The literature of primary carcinoma of the gall-bladder is all of comparatively recent date, the most important contributions having been made within the last five years. By far the largest number have been reported since 1870. Previous to the year 1800 I have been able to find records of but four cases of primary cancer of the gall-bladder. Two of these are mentioned by Stall in 1777, one by Hally in 1786, and one by Baillie in 1794. All of these are included in the series collected in 1890 by Courvosier. During the first half of the present century but nine cases were reported, two of which were probably secondary to cancerous growths elsewhere. The first two of these were in 1839 by Heyfelder, and during the same year Cruvelhier in his "Pathological Anatomy" mentioned the disease, in speaking of the pathology of the gall-bladder, but did not go into a detailed description of the early lesions. The first full account was given in 1840 by Durand Fardel. In this the liver was not involved.

Lazare, in 1847, published a case in which the liver also was free from secondary deposits and was not involved by continuity of growth from the gall-bladder, the most frequent way in which the disease involves neighboring parts. During the same year Notta

published an account of a case. In 1848 Broca, and in 1849 Rippoll, each reported a case to the Anatomical Society of Paris.

Two cases that were probably secondary were that of Burridge in 1845, which is included as primary by Courvosier, but excluded by Musser because of cancer of the breast of some years' standing; and that of Renaud in 1848.

During the next decade (1850 to 1860) nine cases were reported, and the literature was enriched by a number of valuable contributions.

Neschl, in 1852, reported a case, and refers to two others that he had seen, both of which were associated with cholelithiasis. Icereg and Mahieux, in 1853, each published a case. During the remaining years of this decade articles appeared and cases were reported by Klobe, Topinard, Lebert, Pepper, Cassignac, and Markham, the latter describing a remarkable case in a young woman of 28.

From 1860 to 1870 fifteen cases were reported. Wagner in 1863, Gull in 1864, Cornil, Foot and Stokes in 1865, reported cases, though that of the latter was probably secondary. Fraser, Sutton and Buchereau in 1866, Moxon and Paulicki in 1867, Clamets, Murchison and Ogle in 1868, Klebs and Willigkin in 1869, also reported cases. Since 1870 the French, hitherto the chief workers in the field, have given place to the Germans, and scarcely a year has passed but some additional contribution has been made to the subject. During 1870 Villard published the most complete paper that had as yet appeared. He was able to collect and analyze twenty-six cases. Important articles have appeared at different times in Germany by Kohn, Krauss, Lang-Heinrich, and Zenker, who reported eight new cases and collected twenty-eight. Bernheim and Stiller added five new cases to the list. Courvosier devoted a chapter of his "Pathologie und Chirurgie der Gallenwege" to a summary and discussion of 103 cases. In England, Fagge, Moxon, Habershon and Moore have been the chief contributors, while in this country a most interesting and important paper was published in 1889 by Musser, in which he analyzes 100 cases and gives a brief synopsis of each.

Etiology.—Krauss, after analyzing his five cases and those known to him, concludes that hereditary disposition plays no part in carcinoma of the gall-bladder. The first authors who expressed the belief that gall-stones caused carcinoma of the gall-bladder may well be pleased now, on looking over the long lists of cases reported, which again and again demonstrate the truth of their belief. It

seems rather surprising that at the present time we hear the question: Were the gall-stones first, and did they cause the carcinoma, or was the carcinoma first, and did it cause a decomposition of the bile which gave rise to the formation of gall-stones? When but few cases were known this question was well put, but with the material for reasoning at hand it may well be considered as settled. There are a great number of cases of gall-stones without carcinoma of the gall-bladder, but only very few primary carcinomata of the gall-bladder without gall-stones. In secondary carcinoma of the gall-bladder gall-stones are very rarely found, but in primary carcinoma of the gall-bladder their presence is the rule, and there are but few exceptions. These views are well established.

The writer thinks the fact that primary carcinoma of the gall-bladder mainly occurs in females gives strong support to the mechanical theory. Women wear corsets which press the costal arch firmly against parts of the liver, thus increasing the resistance and friction on the anterior wall of the gall-bladder. Orth, in his "Specielle Pathologische Anatomie," Band iii, gives a cut showing carcinoma of the gall-bladder, the latter containing a large stone and the anterior surface of the liver showing a deep indentation. In the accompanying text Orth makes no allusion to the possible rôle which the pressure of the arch may have played in the process, but he undoubtedly has taken it into consideration. In our own case there is also the same change, although less marked; there is an indentation, with thickening of the capsule, and an increase of connective tissue in the liver substance beneath it.

Graham reports a case occurring in a man, a shoemaker by trade, who when at work would sit bent forward, pressing the costal arch against the liver. The position in this case would cause the same pressure on the liver as does the corset in women. Graham evidently did not take this into consideration.

The mechanical theory in reference to carcinomata in general seems to be the only satisfactory one and becomes especially forceful if we review the carcinomata of the alimentary canal and note the typical localizations. There is the carcinoma of the lips which often seems to be caused by the friction of the stems of clay pipes; then the carcinoma of the tongue, for the origin of which sharp-edged teeth are accused; next comes the carcinoma of the fauces, this narrow portion of the oral cavity growing still narrower during the act of swallowing, thus causing a strong friction of the parts with the passing of food. Then the carcinomata of the esophagus, behind the cricoid cartilage and the bifurcation of the trachea,

where a counter-pressure against the food passing by is exerted by the parts named. The cardia is the next principal seat of carcinoma, and the pylorus the next; and it is easy to understand that in these two places increased friction between contents and tissues must take place. This is also the case at the papilla of the common duct, and equally so at the Bauhinian valve, at the hepatic and lienal flexures of the colon, and the rectum down to the anus. All those parts mentioned are fastened to the abdominal walls, or to the vertebral column, or to bones, except the tongue and the lips, which increases mechanical irritation. Of course carcinomata occur in other parts of the intestinal tract also, but even then we often find something interposed which creates essentially the same condition, as, for instance, cicatricial ulcers of the stomach. As Hauser has shown, carcinomata will originate from the margin of such cicatricial ulcers, and I have a specimen which demonstrates this. It shows a large and deep cicatricial ulcer in the pyloric region, and on the margin on the side of the pylorus a carcinoma has developed. When the stomach contracts it tries to throw its contents through the pylorus, and therefore the strongest friction must have taken place just where the carcinoma developed. Chronic inflammatory thickenings, ulcers, stenosis or diverticula can produce the same favorable conditions in other parts of the intestinal tract and thereby favor the growth of carcinomata. It seems to me that a careful study of primary carcinomata in organs where they but rarely occur will throw light on the subject; for example, primary carcinoma of the liver is rather rare, because this organ, if there are no stones in the gall-bladder or the gall-ducts, and if no corset is worn, is but very little exposed to mechanical irritation. If our opinion is right, then something that produces such an irritation should be found in cases of primary carcinoma.

The writer is strongly under the impression that the mechanical factor plays a prominent part in the production of carcinoma. It seems probable that increased resistance of the tissues is not the only important factor to be considered, but that an increase of friction in the intestinal tract by coarse food must also be taken into consideration. If we allow the mechanical theory to reign supreme, we must necessarily pay attention to the kind of food that is most adapted to cause friction. Meat is slippery and fat can also hardly be accused, but meat that is fried hard may act in the way indicated, though only to a very small extent, while it would seem that the carbohydrates are at the bottom of the trouble. Hasty eating, lack of saliva in quantity or quality, or lack of teeth as occurs in old

people, will prevent proper mastication and the conversion of the carbohydrates in the mouth; crusts of bread will add materially, and the imperfectly converted carbohydrates will act like foreign bodies in the relaxed stomach of the aged, and as in the bowels the pancreatic juice, also lessened, will not complete conversion, they may act as foreign bodies all through the intestinal canal. But if we further consider that mechanical factors are also predominant in bacterial invasion, we cannot but take a parasitic theory into consideration, although the œsophagus, cardia, pylorus and some of the other parts named are not at all favored by those micro-organisms which are well known to us; but some of them are, namely, the isthmus faucium, the Bauhinian valve, the cœcum, the colon with its sharp turns and its pockets. The thick epithelial layers of the esophagus, the acid reaction of the contents of the stomach and the duodenum, the quick propulsion of the contents through the small intestines, and the small degree of friction in the latter parts, do not present favorable conditions for bacterial invasion. To prove the great importance of the mechanical factor for bacterial invasion I could bring a good deal of material, not only in reference to the intestinal canal, but also in reference to the larynx, the lungs, the pleura, the pericardium, the kidneys, ureters, bladder, etc. But two examples may suffice. It is well known that the infection of normal valves of the heart takes place at the closing lines, while the free margin of the valves and their basis remain intact for some time. When the blood contains micro-organisms and the valves close, they are pressed into the valvular tissues along the closing lines. Further, some years ago I made a post-mortem examination of a woman who had died of tubercular peritonitis and enteritis. It is well known that in enteritis tuberculosa most of the ulcers are located just before the Bauhinian valve. In this case it was different. There was a diverticulum of the size of a man's fist, about a foot and a half above the Bauhinian valve, and this diverticulum was full of tubercular ulcers, while there were not many between it and the valve, the mechanical factor alone having been removed. However, from all that has been said it seems evident that if parasites unite with the mechanical cause to create carcinoma they must be of a peculiar kind, differing widely from our well known bacteria, especially in their relation to the gastric juice, which exerts such a deleterious influence on the latter.

In reference to the etiology of primary carcinoma of the gall-bladder Musser says: "No facts can be deduced from these cases to aid us in the formation of a theory of the etiology of cancer. Cer-

tain positive relations of probable cause and effect can be pointed out, while in this particular location of carcinoma its greater frequency in the female is established. Of the influence of heredity or occupation, or hygiene, food, drink, or personal habits, climate or country, nothing can be learned.

"Among other causes considered are local injuries, as by a blow (Robinson, Fitzgerald) or a fall (Moxon's case), or the irritation produced by tight lacing. Marquand reports a case of the latter."

Musser gives the following ages at which primary carcinoma of gall-bladder develops: 1 to 10 years, 1; 10 to 20 years, 0; 20 to 30 years, 1; 30 to 40 years, 9; 40 to 50 years, 19; 50 to 60 years, 27; 60 to 70 years, 19; 70 to 80 years, 14; 80 to 90 years, 1; unrecorded, 9; total, 100.

Symptoms.—Krauss calls attention to the fact that in his five cases four patients experienced from the start, and one later, spontaneous pains that could be elicited by pressure in the region of the gall-bladder or at least on the right side of the abdomen. The pains differed in intensity. In three cases a tumor could be felt in the region of the gall-bladder; in the fourth case palpation only occasionally gave a result; and in the fifth case the tremendously enlarged liver covered the enlarged gall-bladder so completely that it could not be felt. In all cases icterus came sooner or later. Disturbances of the intestinal tract existed in all five cases. There was some ascites in the second and fourth cases, but no fever in any of them. The pulse was normal in some, accelerated at times, and in the others slow. Respiration was generally normal, though sometimes accelerated. Cachexia came in all cases earlier or later. The disease lasted from two to eight months.

Musser says that in 100 cases gathered by him, in 68 tumors were discovered in the following locations: In the right hypochondrium of gall-bladder region, in 27 cases; attached to the liver, 10; in umbilical region, 12; in the iliac fossa, 4; in the flank, 2; near the pylorus, 1. Jaundice occurred in 69 cases, and vomiting in 39. There was distinct emaciation noted in 44 cases, diarrhea in 15, fever in 18—due to infectious complications of the bladder or ducts, or to peritonitis or ulceration.

Diagnosis.—Krauss thinks it hard or even impossible in some cases to make a diagnosis *intra vitam* of primary carcinoma of gall-bladder or of carcinoma of the gall-bladder. In many cases a correct diagnosis can be made, if careful repeated examinations are made and if all symptoms receive due consideration. A smooth or nodulated tumor of firm elastic consistency felt in the region of the gall-

bladder, spontaneous pains or pains on pressure in the same region, and cachexia, are the points to be particularly considered. The diagnosis will be supported if the history shows that there has been a cholelithiasis at some time. Icterus, ascites and disturbances of the intestinal tract are only of secondary importance.

In closing, the writer wishes to tender his sincere thanks to Dr. W. G. Knap of Chicago, who has made the microphotographs.

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